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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,704	05/16/2002	Camilo Anthony Leo Selwyn Colaco	8830-21	7595

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Drinker Biddle & Reath
One Logan Square
18th & Cherry Streets
Philadelphia, PA 19103-6996

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,704	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/25/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 16 and 18 have been canceled.
Claims 1-9 and 15 stand withdrawn from consideration.
Amended claims 10-14 and 17 are currently under examination.
1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Please Note: the Examiner of record for the February 16, 2005 Office Action and the Examiner of record for the November 21, 2005 Office Action are/were not the same Examiner.

Response to Arguments for Rejections Maintained

2. Applicant's arguments filed May 25, 2006 have been fully considered but they are not persuasive.

3. . The rejection of claims 10-14 and 17 under 35 U.S.C. 112, first paragraph (Scope of enablement) is traversed on the grounds that: "Claims 10, 11 and 14 have been amended to recite that the heat shock protein complexes are obtained from the heat treatment of pathogenic bacteria. It is believed that this amendment overcomes the Section 112 rejection, particularly in view of the statement at page 7 of the February 16, 2005 office action to the effect that the "specification has adequately described and provided method results and challenge experiments with vaccines comprising one or more complexes between a heat shock protein and an antigenic peptide fragment derived from the heat treatment of bacteria (emphasis added) ."

4. It is the position of the current Examiner that the Scope of enablement in the Office action of dated February 16, 2005 also stated that the heat shock complexes "were also able to generate good immune responses (phase bridging pages 7-8) and went on to state "The results do not directly correlate from one species to another much less to Genus or unrelated organism". While the current Examiner agrees that the instant Specification describes, teaches and shows the

induction of an immune response to heat shock protein/peptide complexes, the immune response induced is not enabled for vaccines and induction of a protective immune response. The current examiner in the Office Action dated November 21, 2005 sought to further provide support for the fact that "The microorganism vaccine art is highly unpredictable (Office Action dated Feb. 16, 2005, page 8, middle of page)."

5. The current Examiner provided evidence of unpredictability in the vaccine art with respect to bacterial heat shock compositions. The compositions were shown to be immunogenic, but not predictably protective against infection by a viable bacterial pathogen. Example 2 of the instant Specification clearly shows the induction of an immune response, and administered **fixed** M. bovis. Fixed M. bovis is non-infective, so the administration showed immune memory, a very high antibody titer over a period of 18 months, but not protection against infection.

6. The scope of enablement rejection is further traversed on the ground of how the claimed vaccine complexes are made, specifically by "heat shock" and sites Example 3 and 4 of the instant Specification in support of the claimed invention, and states "Examples 3 and 4 of the instant application detail the induction of protective immunity against the pathogenic bacteria Myocobacterium tuberculosis, E.coli and Salmonella typhimurium.

7. It is the position of the examiner that the instantly claimed compositions are claimed by product by process claim limitations, and a product produced by a different process that is the same or equivalent composition is encompassed by the claims. Applicant teaches more than one method of obtaining the claimed heat shock protein/peptide complexes and is not limited to the

production of the claimed compositions by heat. Portions of the instant Specification that support the examiner's position follow:

a. at page 6, paragraph 1, the invention is described "and more especially HSP-complexes from these organisms treated by heat shock or other stresses"

b. page 6, paragraph 2 a), "exposing extra-cellular pathogenic organisms to stress inducing stimuli, such as heat"; therefore the invention is not limited to only heat induced complexes.

c. Page 7, paragraph 4 "The extra-cellular pathogen may be one in which the application of an external stress induced the synthesis of stress proteins. However, it is within the scope of the present invention to use pathogenic organisms, for example bacteria, which have been modified, for example genetically engineered, to produce an organism in which the induction or enhancement of the induction of the synthesis of stress proteins occurs constitutively without the need to apply external stresses"; therefore the invention does not require the application of heat to attain the claimed invention.

d. at page 15, instant Specification, lines 4-6 "Non-induced (constitutive HSPs were isolated by centrifugation from the initial cell cultures at 37^{O} C.

8. With respect to Applicant statement that Examples 3 and 4 show induction of protective immunity directed against Mycobacterium tuberculosis, E.coli and Salmonella typhimurium, it is the position of the examiner that Example 3, concludes "Immunisation of mice with the heat-induced HSPs gave significantly better immunity, as assessed by lung colony counts, to live challenge than immunization with constitutive HSPs." Clearly, Example 3 provides support for

the fact that the HSP complexes did not prevent infection, but only reduced lung colonies. Infection by Mycobacterium tuberculosis was not prevented, only reduced. Example 3 does not show the administered complexes to prevent infection, no less provide support that any HSP complex would prevent infection by an pathogenic bacterium.

It is the position of the examiner that Example 4, does not provide support for induction of a protective immune response against challenge, but states "a 10-100 fold antibody titers in the animals immunized with HSPs from heat-induced bacteria as assessed in dot-blot assay using the isolated HSPs". Example 4, teaches an enhanced immune response was induced to the complexes but the immune response was not evaluated for its ability to prevent infection, or to treat already existing infection. Therefore, while Examples 3 and 4 clearly provided support for immunogenic compositions, they do not show the isolated HSP complexes to induce a protective immune response against infection.

The current examiner cited Bae et al who administered GroES/GroEL HtrA proteins in a single composition, the GroES and GroEL proteins form an HSP complex, and this HSP complex/composition was not found to induce a protective immune response, while it was found to be highly immunogenic. (see Bae et al, Section 2.10.2, experimental groups 7 and 8, Figure 1, and Table 2, page 195). Further, the specification fails to provide an adequate written description of what antigenic fragment peptides when associated with a heat shock protein would induce a protective immune response when administered to a animal, by any route, in any amount. While an immune response would be induced because heat shock proteins are known to be highly immunogenic, the skilled artisan would be required to de novo locate, identify and characterize the claimed complexes that would serve as a vaccine composition for any/all

bacteria. This would require undue experimentation given the fact that the specification is completely lacking in teachings as to other surface proteins with the claimed characteristics.

4. ***(Rejection Maintained) Claim Rejections - 35 USC § 102:*** The rejection of claims 10, 11 and 13 under 35 U.S.C. 102(b) as being anticipated by Laminet et al (EMBO Journal. 1990. 9(7): 2315-2319) is traversed on the grounds that Laminet does not teach heat-induced production of GroES or GroEL, but only constitutive expression.

9. It is the position of the examiner that at page 7, lines 29-30 of the instant Specification Applicant teaches the attainment of the invention based upon "the synthesis of stress protein occurs constitutively without the need to apply external stress". What is now claimed is a product by process composition which may be obtained by any process that produces the same or equivalent product and attainment of Applicant's claimed compositions is described to encompass constitutive express of stress proteins. Applicant's traversal is not convincing in light of the guidance, teaching and definitions for the claimed compositions in the Instant Specification.

10. Laminet et al is further traversed by Applicant by stating :
e. Laminet et al used constitutively expressed "heat shock proteins which are less immunogenic" and
f. "teaches neither the formation of a heat shock protein-antigenic peptide fragment complex, or
g. the use of such a complex to induce an immune response."

11. It is the position of the examiner that:

- the claims do not require the claimed compositions to be more immunogenic than

constitutively expressed heat shock proteins. Additionally, at page 7, lines 3-5, the claimed vaccines are defined to include "any composition which stimulates the immune system such that it can better respond to subsequent infections". Therefore any level of immunogenicity, and immune response is encompassed by what is now claimed, and is not limited to the preferred embodiments exemplified in Example 3, nor the embodiments shown in Example 4 of the instant Specification and Examples 3 and 4 of the instant Specification do not show protection against infection upon challenge with a virulent strain of pathogenic bacteria, but show enhance antibody titers (Exp. 4) and reduced numbers of colonies in the lungs (Exp 3). The claimed compositions have not been distinguished from the compositions of Laminet et al which comprise the same or equivalent components, produced by a different process.

12. ***(Rejection Maintained) Claim Rejections - 35 USC § 102***: The rejection of claims 10-14, claims 17 and 18 under 35 U.S.C. 102(e) as being anticipated by Srivastava (US 5,961,979) is traversed on the grounds that:

h. the combination of a mammalian heat shock protein together with a bacterial peptide antigenic fragment is not Applicant invention,

i. points to Examples 3 and 4 in support of the differences between Srivastava and the present claims, and concludes that

j. the process of chemically synthesizing and conjugating results in the product of a heat shock protein/antigen peptide fragment that differs from heat induced heat shock proteins with an antigenic peptide fragment of the instant invention.

13. It is the position of the examiner that while Srivastava claims heat shock protein-antigenic peptide fragment complexes that comprise a mammalian heat shock protein non-

covalently bound to an antigenic peptide from a bacteria, protozoa or fungi, **but** the reference discloses more than just these embodiments.

1. Srivastava's heat shock proteins are not limited to mammalian heat shock proteins. Srivastava discloses DnaK and Hsp70 from E.coli (see col. 5, line 57), and heat shock proteins (see Table 1, col. 16, Hsp60, Hsp70 and Hsp90 from E.coli). The heat shock proteins of Srivastava are defined as "a protein whose intracellular concentration increases when a cell is exposed to a stressful stimuli, it is capable of binding other proteins or peptides and it is capable of releasing the bound proteins or peptides in the presence of adenosine triphosphate (ATP) or low pH." (see col. 11, lines 4-10). The examiner agrees that the antigenic peptide fragment in the complexes of Srivastava are those claimed by Applicant (see Srivastava col. 6, lines 41-45; col. 5, lines 20-22; col. 7, lines 3-5; col. 6, line 67).

2. The stresses described by Srivastava include heat shock stress (see col. 11, line 13), as well as "nutrient deprivation, metabolic disruption, oxygen radicals and intracellular pathogens (col. 11, lines 20-21)."

The instantly claimed compositions are defined by the recited product by process limitations, but may be produced by a different process that produces the same or equivalent product and are not limited to the compositions produced in Examples 3 and 4. Srivastava discloses the claimed compositions produced by a different process, specifically reconstitution. The bacterial heat shock protein (see Table 1 and definitions) is reconstituted to form a complex together with a antigenic peptide fragment from a bacteria, fungus, or protozoa , wherein the heat shock protein is isolated from natural sources or recombinantly produced (see col. 21, line 28) and then complexed with the antigenic peptide fragment that has been "chemically synthesized"

(see col. 21, lines 24-27)" in vitro to generate immunogenic stress protein-antigenic peptide fragment complexes.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594 No side by side comparisons have been submitted to show the novel or unobvious difference between the claimed compositions and the product of the prior art.

7. ***(Rejection Maintained) Claim Rejections - 35 USC § 102:*** The rejection of claims 10, 11 and 13 under 35 U.S.C. 102(e) as being anticipated by Wallen et al (US 5,747,332) is traversed on the grounds that the complexes of Wallen et al are produced by a different process and the instantly claimed complexes the result of stressing a cell by heat shock.

3. It is the position of the examiner that Wallen et al disclose at column 3, lines 49-67, the heat shock proteins may be from prokaryotes, and include the GroEl/GroEs complexes. This embodiment anticipates the instantly claimed compositions. Arguments directed to differing process steps are not convincing because the claimed products are the same or equivalent products produced by a different process. Inherently the reference anticipates the now claimed invention.

4. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition

patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

5. ***Rejection Maintained***: The rejection of claims 10-11, 17 under 35 U.S.C. 102(b) as being anticipated by Yokota et al (1994) is traversed on the grounds that:

a. "The beta subunits of the urease enzyme do not complex with the heat shock protein at the peptide binding site of the heat shock protein" and "the beta subunit components will not be presented to the immune system."

6. It is the position of the examiner that what is now claimed is a complex of a heat shock protein is not required to bind the binding site of the heat shock protein (Additionally, the examiner stated that the complex of Yokota et al comprised both the alpha and beta subunits of H.pylori urease with the heat shock protein). With respect to the beta subunit stimulating an immune response, it is the position of the examiner that the evidence of inherency provided by Evans et al, also provides evidence that all of the components of the complex are immunogenic (see Evans et al, reference incorporated by reference in Yokota et al, Evans page 2125, col. 1, paragraph 2) that states that the 66 K(urease beta subunit), 62K(heat shock protein) and 31 K (urease alpha subunit) are "consistently positive in an enzyme-linked immunosorbent assay" as they immunoreact with immunoglobulin G antibodies in H.pylori infected individuals.

7. The rejection of the claims as anticipated by Yokota et al is further traversed on the grounds that "A key advantage of the present is that the induced heat shock proteins can bind a wide variety of antigenic peptides from a pathogenic bacteria"

8. It is the position of the Examiner, that what is now claimed does not comprise "a wide variety of antigenic peptides", but "an antigenic peptide fragment". Applicant's traversal is not commensurate in scope with the instantly claimed invention as now claimed and is maintained for reasons of record and responses set forth herein.

9. The rejection of claims 10-11, 17 under 35 U.S.C. 102(b) as being anticipated by Eschweiler et al (1993) is traversed on the grounds that Eschweiller et al did not produce the heat shock protein/urease complex by heat shock.

10. It is the position of the examiner that Eschweiler et al disclose the instantly claimed complex, which is claimed by product by process. "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983). The rejection is maintained for reasons of record, and the response set forth herein.

11. The rejection of claims 10-11, 17 under 35 U.S.C. 102(b) as being anticipated by Austin et al (1992) is traversed on the grounds that the urease and heat shock protein do not form a complex through binding of the urease to the binding site of the heat shock protein.

12. It is the position of the examiner that what is not claimed is a complex of a heat shock protein and a peptide of a bacteria, and how they are associated is not claimed. Any type of complex is claimed, no specific mode of complex formation is required by the claims. Therefore the complex of Austin et al that is a combination of a GroEL 60 k bacterial heat shock protein (Helicobacter pylori heat shock protein, see title) complexed with an antigenic peptide fragment (urease) still anticipates the instantly claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

Atlas Powder Co. V.IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. US005561221A US006368599B1 US006500434B1 US005843460A US007041465B1 US006962791B2 US006872542B1 US006913750B2 are cited to show HSPs and proteins, such as FimC/FimH complex and PapD/PapG.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
July 27, 2006

L. F. Smith
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600